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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,606	05/05/2005	Maria Cristina Geroni	17703 (PC27210A)	4724

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EXAMINER	
WEBB, WALTER E	

ART UNIT	PAPER NUMBER
1609	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,606	GERONI ET AL.	
	Examiner	Art Unit	
	Walter E. Webb	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/17/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-27 are pending and rejected.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 16-23 are rejected under 35 U.S.C 101 because the claimed recitation of a use without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. V. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-23 provides for the use of acryloyl distamycin, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 1-7, 9-14, 16-19, and 21-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 9 recite "distamycin or distamycin-like framework", which is unclear and indefinite as it is unclear what is, or is not, a 'distamycin or distamycin-like framework'. The specification defines 'distamycin or distamycin-like framework' as, "any moiety structurally closely related to distamycin itself, for instance by optionally replacing the ending amidino moiety of distamycin and/or its polypyrrole framework, or part of it." (Specification, page 2). The definition is not limiting to any compounds, as it provides only two broad examples of what moieties can be replaced without defining what they are replaced with, and it is further unclear, for example, as to what replacements can be made for the polypyrrole and still be considered 'distamycin-like'.

Further, it is unclear whether the recitation of 'distamycin' in the claims is only distamycin, or whether it embraces the broader definition in the specification.

Claims 9-15 recite, "Products..." which renders the claims unclear and indefinite. The claim first recites the plural products, which embraces more than a single product, and it is unclear whether Applicant is claiming each product individually, or as a group.

Additionally, claim 9 recites, "as a combined preparation for simultaneous, separate or sequential use", which is vague and indefinite, as it is unclear how one formulates a combined preparation for separate or sequential use, particularly in view of the plain meaning of combined which means "a : to bring into such close relationship as

to obscure individual characters : MERGE b : to cause to unite into a chemical compound" (Merriam-Webster Online Dictionary).

Further, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Respectfully, the claims read in light of the specification do not clearly delineate what 'products' are being claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,482,920 (Cozzi) in view of Sironak et al., (Clinical Cancer Research: 2000, 6 (12); 4885-4892).

Applicant claims a composition comprising an acryloyl distamycin derivative of formula (I) and a protein kinase inhibitor (claims 1, 8, 9, 16). The protein kinase inhibitor can be ZD1839 (Gefitinib). Applicant also claims a method of treating tumors and reducing the side effects of cancer treatment with the composition (claims 24 and 26).

Cozzi teaches the acryloyl distamycin derivative of formula I, and a method of treating cancer. (See claims 1-4 and 8-10.) Cozzi also discloses that the acryloyl distamycin derivatives can be combined with an additional antitumor agent for treating cancer or for ameliorating the conditions of mammals, including humans, suffering from cancer. (See col. 13 lines 1-8.)

MPEP § 804 (II) states, "When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. General Foods Corp. v. Studiengesellschafi Kohle mbH, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992). This does not mean that one is precluded from all use of the patent disclosure." (Emphasis added). "Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)."

Thus, in looking to the specification, the specification provides support that protein kinase inhibitors, as anti-tumor agents, would be used in practicing the methods.

Cozzi does not teach a protein kinase inhibitor.

Sironak teaches that protein kinase inhibitors like ZD1839 are very effective cancer fighting agents and suggest significant clinical benefit in combination with a variety of other widely used cancer fighting agents. (See Abstract p. 4885.)

It would have been obvious to a person of ordinary skill in the art to combine the compound of Cozzi with the protein kinase inhibitor of Sironak since they both are used to fight cancer and Sironak suggests significant clinical benefit from ZD1839 in combination with other cancer fighting agents.

Moreover, It is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. (See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).)

Furthermore, it would have also been obvious to a person of ordinary skill in the art that combining the compound of formula I with another cancer fighting agent would lower the side effects of antineoplastic therapy, as per claim 26. The combination, having an additive, synergistic or antagonistic effect, would lower side effects since the individual compounds would be given in lower amounts. It is in the purview of the skilled artisan that toxic side-effects often are intolerable at the dosages required to produce any therapeutic benefits.

Additionally, it was well known at the time of applicant invention that agents in combination having additive, synergistic or antagonistic effects might be expected to shift the dynamics of cell killing toward greater efficiency, and reduce the side-effects by

diminishing the cumulative time of host exposure to a cancer fighting agent. (See Grimley et al., US 6,274,567 at col. 8 lines 42-53.)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cozzi et al. (WO 98/04524, published February 5, 1998) in view of Sironak et al., (Clinical Cancer Research: 2000, 6 (12); 4885-4892) and further in view of Grimley et al., (US 6,274,576).

Applicant claims a composition comprising an acryloyl distamycin derivative of formula (I) and a protein kinase inhibitor (claims 1, 8, 9, 16). The protein kinase inhibitor

can be ZD1839 (Gefitinib). Applicant also claims a method of treating tumors and reducing the side effects of cancer treatment with the composition (claims 24 and 26).

Cozzi teaches the acryloyl distamycin derivative of formula I. (See page 3 lines 25-30 and page 4 lines 1-5; see also examples that follow pp. 4-7.) Cozzi also discloses that the acryloyl distamycin derivatives can be combined with an additional antitumor agent for treating cancer or for ameliorating the conditions of mammals, including humans, suffering from cancer. (See page 20 lines 6-13 and lines 20-29.)

Cozzi does not teach using a protein kinase inhibitor to treat cancer or the inhibitor itself.

Sironak teaches that protein kinase inhibitors like ZD1839 are very effective cancer fighting agents and suggest significant clinical benefit in combination with a variety of other widely used cancer fighting agents. (See Abstract p. 4885.)

Grimley teaches, in the area of cancer chemotherapy, combinations of cell killing agents, including new combinations of dosage strategies, whereby the first agent modulates the cell cycle so as to maximize the toxic effect of the second agent on target cells, while minimizing the toxic effect on non-target cells. Combinations include protein kinase inhibitors (See col. 15 lines 10-35.)

It would have been obvious to a person of ordinary skill in the art to combine the compound of Cozzi with the protein kinase inhibitor of Sironak since they both are used to fight cancer and Sironak suggests significant clinical benefit from ZD1839 in combination with other cancer fighting agents.

Moreover, It is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. (See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).)

Furthermore, it would have also been obvious to a person of ordinary skill in the art that combining the compound of formula 1 with another cancer fighting agent would lower the side effects of antineoplastic therapy, as per claim 26. The combination, having an additive, synergistic or antagonistic effect, would lower side effects since the individual compounds would be given in lower amounts. It is in the purview of the skilled artisan that toxic side-effects often are intolerable at the dosages required to produce any therapeutic benefits.

Additionally, it was well known at the time of applicant invention that agents in combination having additive, synergistic or antagonistic effects might be expected to shift the dynamics of cell killing toward greater efficiency, and reduce the side-effects by diminishing the cumulative time of host exposure to a cancer fighting agent. (See Grimley et al., at col. 8 lines 42-53.)

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 272-1600. The examiner can normally be reached on 9:00am-5:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

WW

MICHAEL MELLER
PRIMARY EXAMINER